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Literature Review

Treatment in transient synovitis cases: A review

Panji Sananta[1*], Fernaldhi Anggadha[1], Eka Noviya Fuzianingsih[2]

1) Orthopaedic and Traumatology Department, Faculty of Medicine Universitas Brawijaya, Saiful Anwar General Hospital, Malang, Indonesia
2) Master of Immunology Study Program, Postgraduate School, Universitas Airlangga, Surabaya, Indonesia

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Correspondence:

panjisananta@ub.ac.id

ABSTRACT

Inflammation of the synovial membrane of a joint is a common symptom of transient synovitis (TS), which is the medical term for a condition that leads to hip discomfort in juvenile patients. The estimated annual incidence of TS is 0.2%, and the risk of developing the disease over one's lifetime is 3%. Unfortunately, the specific pathophysiology of TS is still unclear. Therefore, the particular treatment is still debatable. There are several methods of treating TS, starting with bed rest in the hospital and using analgesics, steroids, skin traction, and joint aspiration. Most of the time, transient synovitis is a self-limiting condition that heals independently and is managed conservatively by monitoring and rest. Several medical therapy options, including analgesics, NSAIDs, and corticosteroids, speed up healing. On the other hand, skin traction is also reported to provide beneficial therapeutic effects for TS patients. Thus, with many therapeutic options, TS's "golden" management still needs further study.

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INTRODUCTION

Synovitis is an inflammation of a joint's synovial membrane that causes joint pain, swelling, warmth, and erythema. Synovitis can result in joint damage or destruction, deformity, and loss of function (Sokoll and Helliwell, 2006; Lipshaw and Walsh, 2022). Hip discomfort is frequently brought on by transient synovitis (TS), particularly in the patient population of children (Whitelaw and Varacallo, 2022).

While the specific mechanism of transient synovitis is unclear, it is frequently associated with upper respiratory virus symptoms and often lasts (McCarthy and Noonan, 2008). Other researchers, on the other hand, have identified several potential causes, including trauma and hypersensitivity (Nouri *et al.*, 2014). Synovitis has been arbitrarily determined to be temporary if it resolves within 12 weeks. It is considered chronic if it does not go away after 12 weeks, recurs, or imaging shows signs of damage (erosions). Even though this article is about transient synovitis, risk factors for chronic disease and early treatments for chronic illness will be discussed. Boys are twice as likely as girls to experience transient synovitis, which often affects children between the ages of 3 and 8 years (Pauroso *et al.*, 2011).

Transient synovitis is usually harmless and self-limiting, whereas persistent synovitis can be painful and debilitating. The goal of screening people recently diagnosed with synovitis is to identify those at risk of developing damage and disability so that appropriate treatment can begin. This therapy window is less than three months after the onset of symptoms (Morel and Combe, 2005). The goal of transient synovitis treatment is to alleviate symptoms while also encouraging synovitis healing. In patients with risk factors for chronic disease, the goal is to limit disease mechanisms and prevent progression to chronic synovitis. Ideally, this will result in the illness "turning off" and the patient entering remission (Sokoll and Helliwell, 2006).

In this review study, we will describe the main features of transient synovitis to distinguish it from other possible causes of acute hip pain in children, especially septic arthritis (SA), which in several diagnoses shares similarities with transient synovitis. With the suitable characteristics and the proper diagnosis, it can determine the appropriate treatment for patients with transient synovitis. This review intends to present the most comprehensive analysis of the current management of TS cases, incorporate new changes since its previous assessment, and provide a brief overview of the accumulated findings over the years.

METHOD

The method used in this paper is a literature review study. The source search databases are PubMed, Science Direct, and Google Scholar. The article search collected topics on the "treatment of transient synovitis". The range inclusion of the literature was published from 2013-2023 in English by choosing the full article journal and literature review. The search keyword is "treatment in transient synovitis". The total number was 6 out of several that met the inclusion criteria.

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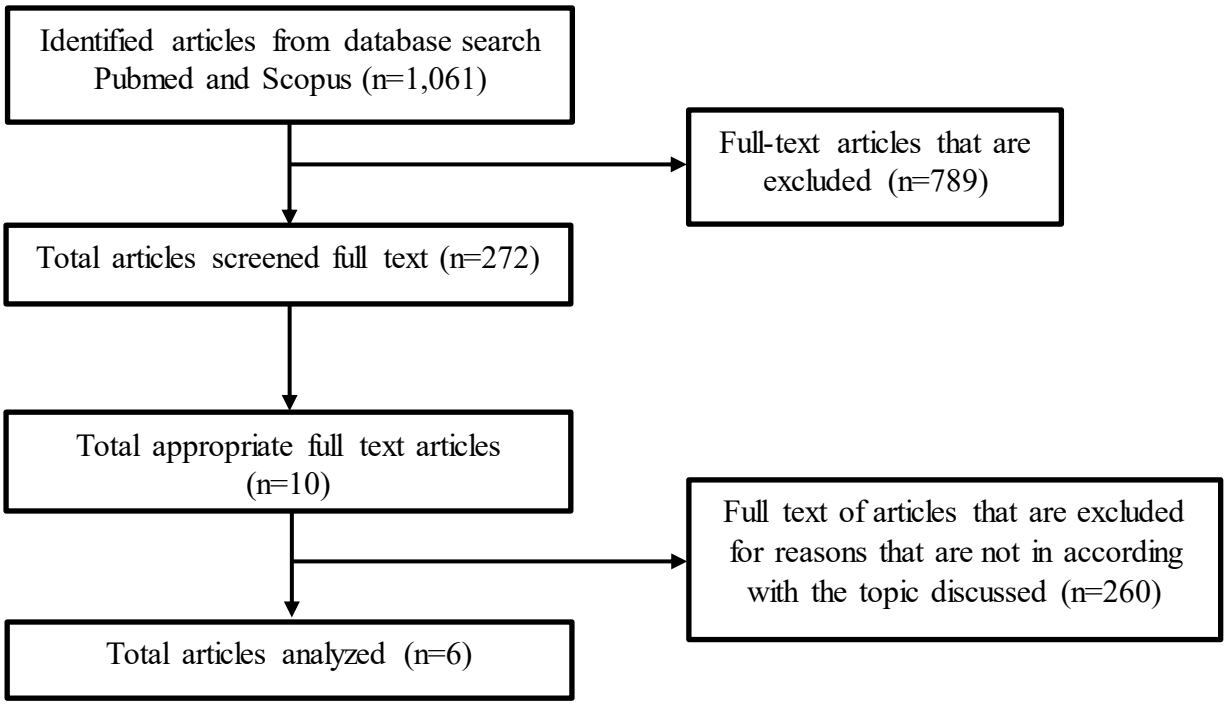

Figure 1. Information Analysis

LITERATURE REVIEW

Epidemiology

Pediatric hip pain has a wide range of diagnoses, ranging from benign diseases to surgical complications. Consequently, TS is not considered a valid diagnosis, even though it is the condition that occurs the most frequently. Osteomyelitis, septic arthritis, primary or metastatic lesions, slipping capital femoral epiphysis (SCFE), and Legg-Calve-Perthes disease (LCPD) are all illnesses that have the potential to be lethal if they are not treated as soon as possible (Nouri *et al.*, 2014). The annual incidence of TS and the lifetime risk of developing the condition are estimated to be 0.2% and 3%, respectively (Lennart, 1983). Transient synovitis is most prevalent in children between three and eight (Baskett *et al.*, 2009). According to a recent study conducted in the Netherlands, the mean and median onset ages were determined to be 4.7 and 4 years, respectively (Krul *et al.*, 2010). Additionally, the fact that males are more likely to be affected by TS is inconsistent with a viral origin. In children diagnosed with transient synovitis, biochemical research has been unable to establish a causal relationship between the disorder and viral infection (Harrison *et al.*, 2014).

The cause of TS is unknown as of yet. There will be several possibilities put forth, but none of them have received solid evidence. It is suggested that there are three risk factors: trauma, past bacterial infections, and respiratory tract infections. Many pediatric patients arrive having recently experienced trauma or having a history of URI symptoms. Patients who have TS are more likely to have had viral symptoms in the past, such as throwing up diarrhea or even the common cold

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(K Katherina, 2010). Another study found that TS levels fluctuate throughout the year, with higher levels recorded in October and lower in February. Studies try to hide the existence of viral diseases, such as human herpes simplex virus 6 and parvovirus B-19. Other potential risk factors include drug-induced hypersensitivity reactions as well as allergic reactions. The pathology causing TS remains unknown. The suggested pathogenic cascade involves non-specific inflammation of the synovial joint lining to generate hypertrophic alterations. The acute inflammatory phase is characterized clinically by discomfort that disappears within 24 to 48 hours (Whitelaw CC, 2022).

Research findings indicate that the emergence of TS is associated with an elevated likelihood of relapse, with an estimated yearly relapse frequency of 4%. This translates to a 20-fold escalation in risk compared to the risk observed in the broader population (Lennart, 1983). Nonetheless, reliable epidemiological data are limited, highly variable, and primarily derived from Asian nations, restricting their generalizability.

Diseases Related to Transient Synovitis

Septic arthritis (SA), Lyme arthritis (LA), and Legg-Calve-Perthes disease (LCPD) are diseases whose symptoms and diagnosis are similar to transient synovitis. There are several significant differences between the three diseases from a clinical point of view, consisting of laboratory tests and radiographic examinations (Cook, 2014).

Children aged <2 years are more likely to have SA. Meanwhile, children over the age of 9 have a slight chance of experiencing SA or TS. The three to eight years of age presents the most significant diagnostic difficulties for both disorders. Meanwhile, LCPD disease ranges between 3 and 10 years, similar to TS. Some similarities between the two diseases are the variable onset of hip pain, limping, limited movement, and fever (Cook, 2014). In addition, in SA patients, the patient did not have a prior respiratory tract infection, whereas 29% of TS patients had a previous respiratory tract infection. All patients with SA could not bear weight, compared to 52% of TS patients who could still maintain weight (Tay *et al.*, 2013).

Trauma is expected at the onset of symptoms of these three diseases, for which there may be more than one diagnosis. In TS and SA, the incidence of trauma at the beginning of symptoms is mild, whereas in LCPD, the event of trauma is less likely, perhaps some distance from the onset of symptoms. Transient synovitis and Septic arthritis are characterized by a comparatively brief duration of symptoms lasting a few days. Conversely, LCPD typically manifests over an extended period ranging from weeks to months. Occasionally, a recurrence of TS disease may indicate LCPD disease. Patients diagnosed with TS and SA conditions typically report experiencing pain levels ranging from moderate to very severe.

Conversely, individuals with LCPD tend to exhibit a lower incidence of severe pain. Transient synovitis and septic arthritis may manifest as weight-bearing refusal, whereas LCPD does not typically show this symptom. The LCPD ailment frequently manifests as a tendency to lean towards the impacted side while standing or a gait characterized by a rigid hip (Cook, 2014). The body temperature in SA disease is <39.12 ^{0}C, while in TS there is a mild fever <37.2 ^{0}C, and in LCPD disease, fever is not a feature of the disease (Tay *et al.*, 2013).

Laboratory tests for these three diseases include the complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). In TS disease, the WBC count is average (<12 x 10^9/L), the ESR is <40 mm/H,

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and the CRP is normal (<20 mg/L). In SA disease, the WBC is > 12 x 10^9/L, the ESR is > 40 mm/H, and the CRP is > 20 mg/L, whereas in TS disease, all laboratory parameters are normal (Cook, 2014).

An ultrasound examination is performed to identify the presence or absence of effusion. An effusion is considered to have occurred when the distance between the bone and the capsule exceeds 2 mm. The diagnosis of SA cannot be advocated by some for ultrasonography because of controversy over the ability of ultrasonography to differentiate septic and purulent effusions from inflammatory effusions. The use of MRI is reported to be able to distinguish between TS and SA. The best indication for this MRI examination is that the possibility of SA has been addressed under challenging cases after an acute problem (Cook, 2014).

Lyme arthritis is frequently observed to manifest in the knee joint. This disease is similar to SA and TS. According to Cruz, Jr. *et al.* (2018), systematic review and meta-analysis, the mean WBC count for LA is 10.6 x 10^9/L, the mean ESR value is 41 mm/H, and the mean CRP value is 3.9 mg/L. The peripheral WBC is not a dependable laboratory indicator for discriminating between SA and TS. However, the ESR can aid in identifying patients who necessitate additional laboratory examinations such as serum Lyme titers or intra-articular hip aspiration. The clinician should consider obtaining synovial fluid for SA evaluation when patients exhibit an ESR exceeding 40. According to Cook (2014), Lyme serology may increase ESR levels below 40 mm/H due to the possible occurrence of LA or TS. Children who suffer from Lyme arthritis experience bouts of oligoarthritis that are typically only a few days long but come back frequently. The knee is the joint most commonly affected by LA, but hip involvement is uncommon (Dubois-Ferrière *et al.*, 2015).

Diagnosis

Clinical Presentation

Transient synovitis is characterized by sudden and severe pain in the groin or thigh region, accompanied by a limp or aversion to weight-bearing activities. The manipulation process results in inconsistent degrees of flexion, abduction, and external rotation in the impacted hip while in a relaxed position, accompanied by a restricted passive range of motion (Kastrissianakis and Beattie, 2010). This position may be more comfortable due to lower intracapsular pressure. A minority of people can participate in bilateral activities. There may be a low-grade fever on occasion. Usually, the temperature is below 38 °C. Elevated temperatures suggest that the hip discomfort is not attributable to benign synovitis (Do, 2000).

The diagnostic procedure is intricate due to the lack of distinct laboratory indicators, unfavorable laboratory findings, and the necessity to rule out knee or lumbar spine discomfort as the underlying cause of the symptoms (Vijlbrief *et al.*, 1992; Ehrendorfer *et al.*, 1996). Various histories may be necessary before the presentation because of the diverse proposed etiologies. A medical history of a middle respiratory illness, gastrointestinal system infection, urinary tract infection, or minor trauma could provide valuable insight (Lennart, 1983).

The study conducted by Taylor and Clarke involved the examination of 509 patients who presented with a limping gait and hip irritation. The primary objective of the study was to establish clinical criteria that could be used to differentiate between transient synovitis and septic arthritis. The study revealed that severe pain and spasms were present in 11.5% of cases of TS and 61.9% of cases of SA. Similarly, soreness on palpation was observed in 17.2% of cases of TS and 85.7% of cases of SA. A temperature greater than 38 °C was found in

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7.9% of cases of TS and 81% of cases of SA. Additionally, an ESR greater than 20 mm/h was identified as a significant variable in 10.9% of cases of TS and 90.0% of cases of SA. Septic arthritis can be indicated by the presence of any of these clinical criteria, given a sensitivity of 95% and a specificity of 91% (Taylor and Clarke, 1994).

Magnetic Resonance Imaging (MRI)

Besides clinical factors, novel imaging techniques have emerged for evaluating and diagnosing sudden hip discomfort and excluding SA. The methods mentioned in the text are power Doppler sonography, gadolinium-enhanced MRI, and pinhole collimation scintigraphy, as reported by Strouse *et al.* (1998) and Lee *et al.* (1999). Despite the typically average results, medial joint space enlargement may be revealed in patients suspected of having TS, necessitating the continued use of plain radiographs (Baskett *et al.,* 2009).

The efficacy of MRI in discriminating between TS and SA has been demonstrated, wherein the former is characterized by contralateral joint effusion and the absence of signal-intensity anomalies in the bone marrow (Yang *et al.*, 2006). Kwak reported that septic arthritis was more likely to have reduced perfusion at the femoral epiphysis on fat-suppressed gadolinium-enhanced coronal T-weighted MRI than TS (Kwack *et al.*, 2007). Magnetic resonance imaging may be used in patients with ambiguous clinical presentation and ultrasound findings. Magnetic resonance imaging facilities are typically inaccessible, necessitating the administration of general anesthesia. Moreover, considering the comparatively subdued nature of transient synovitis, MRI may not be the most feasible approach for determining a diagnosis (Nouri *et al.*, 2014). Joint effusion will occur in most SA and TS patients with an insignificant degree of joint effusion. However, contralateral hip joint effusion is more frequently found in TS compared to SA (Adam *et al.*, 2022).

Joint Aspiration

It is recommended that patients with a moderate-to-high likelihood of SA undergo hip aspiration guided by fluoroscopy, as discontinuing treatment may lead to unfavorable outcomes (Nouri *et al.*, 2014). According to Kung *et al.,* the hip was inserted utilizing conventional fluoroscopic examination methods employing an 18-20-G spinal needle. The authors elucidate that contrast is unnecessary in cases of fluid aspiration as the presence of fluid can be deduced from the joint by placing the needle tip on the femoral neck and verifying this through fluoroscopic examination. When the synovial fluid was not aspirated, the authors described the instillation of 10 ml of iothalamate meglumine contrast or non-bacteriostatic saline through injection, followed by inhalation. The authors administered a small quantity of Conray 60 to confirm the intraarticular positioning in instances where saline was used for lavage (Kung *et al.*, 2012).

DISCUSSION

Treatment

Several methods of treating TS, from bed rest in the hospital, using analgesics, steroids, and skin traction, to joint aspiration (Sokoll and Helliwell, 2006; Nouri *et al.*, 2014).

Hospitalizations

Transient synovitis is a condition that is characterized by self-limitation and spontaneous resolution and is typically managed conservatively through rest and monitoring. Furthermore, TS is typically treated with rest and anti-inflammatory medications (Do, 2000). Many studies emphasize bed rest's importance in transient synovitis when combined with

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other treatment options. Bed rest, on the other hand, is used as a mandatory therapeutic option that must be followed to achieve the desired therapeutic goals (Asche *et al.*, 2013).

Analgesics

The primary symptom of transient synovitis is pain, and analgesics are the first line of treatment. If the symptoms persist, analgesics will be given continuously. Many analgesics are now non-proprietary and available without a prescription; paracetamol is the most common example. If this is insufficient, higher doses of prescription-only opiates like codeine (in co-codamol), dihydrocodeine, tramadol, and nefopam may be required. Nausea, vomiting, sleepiness, and constipation are common side effects (Sokoll and Helliwell, 2006). Transdermal analgesic medications (e.g., fentanyl and buprenorphine patches) are available and valuable in the treatment of established arthritis because they provide adequate analgesia with fewer side effects such as nausea, constipation, and drowsiness (Ahmedzai and Brooks, 1997).

The majority of scholars endorse the utilization of nonsteroidal anti-inflammatory drugs (NSAIDs). In 2002, Kermond et al. conducted a triple-blind, randomized, placebo-controlled study to assess the effectiveness of ibuprofen in reducing the duration of symptoms. The study revealed that the average number of days with symptoms decreased from 4.5 days in the placebo group to two days in the ibuprofen group. Notably, transient hip synovitis typically resolves within five to seven days without intervention (Kermond *et al.*, 2002). NSAIDs typically provide quick and effective symptom relief in the context of inflammatory symptoms. The NSAID response is part of the clinical assessment of inflammatory synovitis (Sokoll and Helliwell, 2006).

NSAIDs are highly effective in the treatment of symptoms associated with inflammatory synovitis because they act as both analgesics and anti-inflammatory medications. However, negative consequences have limited its use. The most serious is gastrointestinal ulceration (not only upper GI ulceration but also ulceration in the small and large bowels). In a 1988 study, NSAIDs were discovered to be the leading cause of hospitalization in elderly patients with bleeding or perforated ulcers. Recent research has shown that both conventional and COX-2-selective NSAIDs cause a time- and dose-dependent increase in cardiovascular risk (Hippisley-Cox and Coupland, 2005).

NSAIDs are positioned as adjuvant short-term treatment in the initial phase of synovitis (i.e., the patient waiting to see a rheumatologist), as well as for flares and recurrences, due to NSAIDs toxicity and the widespread and increasingly earlier use of disease-modifying antirheumatic drugs (DMARDs) in persistent synovitis, which results in better control of the underlying disease process. Long-term use should be avoided whenever possible to reduce the risk of adverse effects (Sokoll and Helliwell, 2006).

Corticosteroids

Corticosteroids are potent anti-inflammatory drugs with immunosuppressive properties. Their rapid onset of action (24-48 h) and good safety profile (if taken short term), as well as the variety of administration methods (intra-articular, intramuscular, and oral), justifies their widespread use in more severe synovitis, usually after NSAIDs. Because of their immunosuppressive effects, concomitant infections must be ruled out before using them (Sokoll and Helliwell, 2006).

Corticosteroids have been shown to reduce the development of radiographic erosions following intra-articular or systemic administration. If there are fewer than five affected joints, intra-articular administration is recommended

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because the local effect is more significant and the systemic effects are less severe. The intra-articular injection dosage varies with joint size. If more than two or three joints are affected, intramuscular methylprednisolone or triamcinolone treatment is more effective and preferable to oral therapy because weaning patients off corticosteroids is less risky.

Corticosteroids exhibit varying half-lives, namely short, intermediate, or long, associated with their anti-inflammatory properties. These properties include upregulating anti-inflammatory genes and downregulating various inflammatory genes, including cytokines and enzymes (Tjandra and Pradipto, 2019).

Skin Traction

In most orthopedic cases, traction is still the first line of treatment for trauma and infection. Traction is the use of a pulling force to accomplish one or more of the following goals: to prevent or reduce muscle spasms; to immobilize, rest, or regulate the mobility of a joint or body part; to minimize, realign, and immobilize a fracture or dislocation and maintain its alignment; and to elevate a limb to reduce edema (Duperouzel *et al.,* 2018).

According to several studies, skin traction can be combined with analgesics or nonsteroidal anti-inflammatory drugs (Uziel *et al.*, 2006). According to studies, skeletal traction can reduce significant pain and accelerate inflammation healing (Skinner *et al.*, 2002; Uziel *et al.*, 2006). Most patients with transient synovitis were pain-free within a few days of admission. In cases of transient synovitis, traction is usually removed after 5-7 days (Terjesen and Anticevic, 2018).

Prognosis

Benign TS disease can heal without treatment over 3–10 days. When a patient is diagnosed with TS, it will be followed by serial clinical examinations and ultrasonography to determine the resolution of symptoms and effusions that occur in most patients after one week of TS. It should be noted that there is a possibility of recurrence in reported conditions with previously documented diagnoses (Nouri, A., D. Walmsley, B. Pruszczynski, 2014). The recurrence rate for TS disease ranges from 20–25%. During the examination period, it is recommended to provide the patient with information regarding the heightened likelihood of recurrence associated with the diagnosis of TS. A single study has documented transient synovitis recurrence rates at various follow-up intervals. Specifically, the study reported recurrence rates of 69%, 13%, and 18% at one-year, two-year, and long-term follow-up periods, respectively (Whitelaw CC, 2022).

CONCLUSION

The etiology of acute hip pain in pediatric patients is often attributed to transient synovitis. However, there remains a significant gap in knowledge regarding this condition. There exist indications that the likelihood of an infection being viral is plausible, yet this notion remains controversial. Hence, the precise course of treatment remains a topic of ongoing debate. Nevertheless, using a combination of bed rest or immobilization with NSAIDs or steroids is commonly employed and has yielded a satisfactory outcome.

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